Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 114, 124, 125, 127, 129-131, 133-137, 139, 140, 215, and 230-233 are pending in the application, with claim 114 being the independent claim. Claims 121-123, 126, and 128 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 231-233 are sought to be added. Support for these amendment can be found, *inter alia*, on page 10, lines 8-17; page 54, line 4 through page 56, line 25; page 60, lines 7-8; and page 62, lines 7-16; and in the Examples. Amendments to the specification have been made to correct typographical errors and to conform with U.S.P.T.O. requirements. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Information Disclosure Statement

The Examiner has stated that he did not receive a Form PTO-1449 with the First and Second Supplemental Information Disclosure Statements filed July 10, 2003. Applicants submit herewith a copy of the Forms PTO-1449 filed July 10, 2003 and respectfully request that they be initialed and returned.

Objection to the Specification

The Examiner has objected to the specification for an improper sequence designation, though he noted that the designation is correct in the sequence listing. Specifically, the use of "X" and "a" in the paragraph beginning on page 54, line 26 was objected to as being improper. Applicants have amended this paragraph to use the proper designations and respectfully request that this objection be withdrawn.

The Examiner has also objected to the specification for failing to properly demarcate the trademark GENBANK™ on page 10, line 4. Applicants note that GENBANK has been registered and therefore have amended this paragraph to recite GENBANK®, as well as the paragraph beginning on page 69, line 2, which also recites this term. Likewise, PADRE has been registered and the appropriate amendments to the specification have been made to indicate this as well.

The Examiner has objected to the specification for containing the typographical error "of to" in line 10 of the amended priority claim. Applicants have amended the priority claim by deleting "to" in order to correct this typographical error in lines 1 and 10.

The Examiner has objected to the specification for failing to provide antecedent basis for the term "linker" in claims 129 and 135 in the proper context. Without acquiescing to this objection, Applicants have deleted "linker" from claims 125 and 139, which now recite "linked by a spacer molecule" or "linked by one or more spacer amino acids". Support for this amendment can be found on page 54, lines 4-15.

All objections to the specification have been accomodated, obviated or rendered moot. Therefore, Applicants respectfully request that the objections be withdrawn.

Substitute Sequence Listing

The Examiner has required that the sequence listing be amended per the Notice to Comply (copy filed herewith). Specifically, the Examiner has required that the description for SEQ ID NO:6698 be amended so that the alanine at positions 1 and 13 is correctly identified as L-alanine or D-alanine. Applicants submit three copies of compact discs containing the corrected substitute sequence listing with the appropriate amendment herewith. Applicants respectfully request that the requirement be withdrawn as it has been fulfilled.

Rejections under 35 U.S.C. § 112, first paragraph, Written Description

Claim 133

Claim 133 was rejected under 35 U.S.C. § 112, first paragraph for allegedly lacking written description. Specifically, the Examiner asserted that the term "and a liposome" was not supported in the specification. Applicants respectfully traverse this rejection as it may be applied to the amended claim.

Claim 133 has been amended to recite "which is incorporated as part of a liposome". Literal support for this phrase can be found on page 60, lines 7-8. This amendment was made solely to reword the claim so its support was more readily apparent. As the support for the amended claim is literal, Applicants assert that it has written description support. Therefore, Applicants respectfully request that the rejection be withdrawn.

Claims 114, 121, 122, 124-131, 133-137, 139, 140, 215 and 230

Claims 114, 121, 122, 124-131, 133-137, 139, 140, 215 and 230 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description support. Specifically, the Examiner alleged that the claims encompass a diverse genus of peptides that is not supported by the specification. Applicants traverse this rejection as it may apply to the amended claims.

The test for the written description requirement is whether one skilled in the art can reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. The Federal Circuit has re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [they] invented what is claimed,'" *Union Oil of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000). Furthermore, an Applicant is not required to explicitly describe the subject matter. *Unocal*, 208 F.3d at 1000; *see also* M.P.E.P. § 2163.02 ("The subject matter of the claim need not be described literally (*i.e.*, using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement."). The Court emphasized the importance of what the person of ordinary skill in the art would understand from reading the specification, rather than whether the specific embodiments had been explicitly described or exemplified. Indeed, as the court noted, "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Unocal*, 208 F.3d at 1001.

Applicants note that the Federal Circuit stated in *Univ. of Calif. v. Eli Lilly & Co.*, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997), that:

> A description of a genus of cDNAs may be achieved by means of a recitation of [1] a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or [2] of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus . . . We will not speculate in what other ways a broad genus of genetic material may be properly described . . .

Univ. of Calif., 43 U.S.P.Q.2d at 1406. Thus, the Federal Circuit has stated that the written description requirement for a claim directed to a genus of cDNAs may be satisfied by providing the sequences of a representative number of cDNAs which fall within the scope of the genus or by providing a recitation of structural features which are common to a substantial portion of the members of the genus. *Id.*

The claimed peptides of the present application are biomolecules analogous to the cDNAs of *Univ. of Calif.* for which the Federal Circuit has stated that a common structural feature can satisfactorily support a genus of cDNAs. For the reasons stated below, Applicants assert that the disclosure of SEQ ID NO:6827 as the common structural feature as well as the disclosed additional features of the claimed invention satisfies the written description requirement.

Without acquiescing to the rejection, claims 121, 122, 126, and 128 have been cancelled. Claim 114 has been amended to a peptide consisting of SEQ ID NO:6827. This peptide is clearly supported in the specification, particularly in the sequence listing. Each of the claims requires the sequence of SEQ ID NO:6827, so one of skill in the art

would be easily able to identify members of the genus claimed herein. Each member will contain the unique sequence of SEQ ID NO:6827. Additional limitations of the dependent claims, such as a T helper peptide, spacer molecules, etc., are well known in the art and described in detail in the specification. As required by *Unocal*, a person of skill in the art would be able to derive the claimed invention based on the novel peptide of SEQ ID NO:6827 and disclosure in the specification. Applicants respectfully assert that the written description requirement has been fulfilled.

Example 8 of the Written Description Guidelines further supports Applicants' assertion. This example is directed to a claim comprising SEQ ID NO:2, which, according to the Example, is taught in the specification. Analysis of this claim is summarized on page 35 of the Guidelines as follows:

> Weighing all factors including (1) that the full length ORF (SEQ ID NO: 2) is disclosed and (2) that any substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution, taken in view of the level of knowledge and skill in the art, one skilled in the art would recognize from the disclosure that the applicant was in possession of the genus of DNAs that comprise SEQ ID NO: 2.

Synopsis of Application of Written Description Guidelines (U.S.P.T.O), page 35.

In the present case, SEQ ID NO: 6827 is disclosed, and any variability within the genus arises due to addition of elements that are not part of Applicants' particular contribution. T helper peptides, spacer molecules and the like were well known in the art as well as disclosed in the specification. Applicants assert that one of skill in the art

would readily recognize Applicants' possession of the claimed invention. Therefore, Applicants respectfully request that the rejection be withdrawn.

If the Examiner takes the position that the claimed peptide is not analogous to Example 8 of the Guidelines because the claimed peptide is drawn to a short peptide epitope, Applicants respectfully point out that both SEQ ID NO:2 of the Guidelines and SEQ ID NO:6827 of the claimed invention are complete *functional* units. In particular, SEQ ID NO:2 of the Guidelines encodes a polypeptide of interest, and SEQ ID NO:6827 of the present invention is a peptide with a complete CTL motif.

Moreover, even absent this analogy, Applicants draw the Examiner's attention to *Ex parte Fisher*, a non-binding decision of the Board of Patent Appeals and Interferences (Appeal No. 2002-2046; heard March 16, 2004; provided herewith as Attachment A). This recent decision, while non-binding on the Board, provides guidance with respect to the Board's thoughts on molecules comprising short sequences, in this case, ESTs. As the Examiner is aware, ESTs are short nucleotide sequences randomly selected from cDNA libraries. The claim at issue in *Fisher* was drawn to a substantially purified nucleic acid molecule encoding a fragment of a maize protein comprising a nucleic acid sequence selected from a group of five EST sequences. Although nothing was known of the peptide fragments encoded by these sequences and the claim used the open transitional phrase "comprising", the Board held that there was adequate written descriptive support in the specification and overturned the Examiner's 112, first paragraph, rejection. The Board stated "[t]hat the claimed nucleic acid molecules may have other molecules attached to either, or both of their 5' or 3' ends does not diminish appellants' adequate written description of the nucleic acids [*sic*] molecules with the sequence set forth in SEQ ID NO:1 through SEQ ID NO:5." *Id.* at page 26.

Applicants submit that the present claims do not read on a genus more varied than that encompassed by a nucleotide sequence comprising an EST sequence. As the Board has held that such claims have adequate written description on the basis of the disclosed EST sequence information, Applicants assert that the instant specification contains at least as much support and the rejection should be withdrawn.

Finally, the Examiner cited Schoel as a reference showing varied binding characteristics of epitopes of different lengths and asserted that this reference shows the highly variable nature of the claimed genus as one potential common function (binding) may differ. Applicants respectfully remind the Examiner that the claims do not require a particular binding capability, but instead relies on a common structural feature (the sequence) to define the members of the claimed genus. However, assuming *arguendo* a particular binding characteristic is required to identify members of the claimed genus, Applicants assert that a person of skill in the art would be able to identify this binding characteristic in candidate molecules using the detailed techniques disclosed in the specification, especially in Examples 1-3. As discussed in more detail in Applicants' argument below addressing the enablement rejection, it is routine to screen even a large number of candidates given the knowledge in the art and the guidance in the specification. Thus, the skilled artisan would easily be able to recognize that Applicants have invented what is claimed as required by *Unocal*.

Importantly, Applicants assert that the addition of additional molecules to the peptide does not necessarily affect its binding. Indeed, for the claimed peptide to bind to an HLA, it is first processed inside the cell prior to association with the appropriate HLA. It was known by the earliest claimed priority date that these epitopes are typically processed from larger proteins by intracellular proteosomes that recognize cleavage sites

adjacent to the epitope, thus allowing binding of the processed epitope to HLA. Del Val *et al.*, *Cel*l 66:1145-1153 (1991) (of record as document AS16); Eisenlohr *et al.*, *J.Exp.Med.* 175:481-487 (1992) (of record as document AT17). Del Val *et al.* produced chimeric proteins containing a known epitope at different positions within an unrelated protein. Del Val *et al.*, abstract. They found that although the yield of processed epitope differed depending on the positioning of the epitope within the chimera; nonetheless, the chimeras *were* correctly processed to produce the epitope. *Id.*, abstract and 1149, col. 2, 3d full paragraph. Eisenlohr *et al.* also showed that flanking residues influence epitope processing. Eisenlohr *et al.*, abstract. They also showed that the "the effect of negatively acting flanking sequences can be overcome by additional flanking sequences." *Id.*, 485, col. 2, 3d paragraph. The results of Del Val *et al.* and Eisenlohr *et al.* were reviewed in Yewdell and Benninck, *Adv. Immunology 52*:1-123 (1992) (of record as document AR29). Yewdell and Benninck summarized other studies in which epitopes were placed in recombinant proteins and were able to be processed no matter where they were located. Yewdell and Benninck at 31-32. Finally, a multiepitope vaccine involving HIV antigens is in clinical trials, demonstrating that more than one epitope can clearly be used to generate an immune response. *See* Epimmune Inc. website (http://www.epimmune.com/technology/vaccine programs.cfm).

Therefore, including additional flanking molecules would not normally prevent binding of the cleaved peptide (SEQ ID NO:6827) to the HLA peptide binding domain as they will be removed during processing. Indeed, like in Del Var *et al.* and Eisenlohr *et al.*, the specification discloses that spacer molecules that facilitate such cleavage can be used to enhance epitope presentation (page 49, lines 19-20). Clearly, many epitopes

capable of retaining their function within the context of a larger peptide or molecule are well known in the art.

In view of the above evidence, Applicants assert that the written description requirement for the claimed invention is amply met by the specification and the state of the art at the time of filing. Therefore, Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph, Enablement

Claims 114, 121-131, 133-137, 139, 140, 215 and 230 were rejected under 35 U.S.C. § 112, first paragraph for allegedly not being enabled. Specifically, the Examiner asserts that "to make the claimed invention, the skilled artisan would first have to perform an undue amount of additional experimentation to determine which of the claimed peptides or proteins, and compositions thereof, can be used to stimulate an immune response that correlates with tumor clearance". Office Action, page 10. Additional uses recited by the Examiner include stimulating an immune response in a patient, analyzing immune responses against the claimed peptides, and as a vaccine for treating prostate cancer. *Id.* at pages 11 and 13. Applicants respectfully traverse the rejection as it may be applied to the amended claims.

In order for a claim to be enabled, the specification must teach one of ordinary skill in the art to make and use the invention without undue experimentation. The factors that can be considered in determining whether an amount of experimentation is undue have been set forth in *In re Wands*, 858 F.2d731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: 1) the guidance provided by the specification; 2) the amount of pertinent literature; 3) the presence of working examples; and 4) the

predictability of the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. *See id.*

It appears the rejection is one based on "how to use" since the current claims are drawn to peptides and compositions, not methods. Applicants remind the Examiner that

> [W]hen a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire score of that claim is sufficent to preclude a rejection for nonenablement based on how to use . . . if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention.

M.P.E.P. § 2164.01(c).

The instant claims are not limited by a recited use, so any enabled use disclosed in the specification enables the claims if the use is in keeping with their scope. Without disclaiming or disparaging any of the uses disclosed by the specification, Applicants note that the enablement requirement does not require data showing tumor clearance, treatment efficacy or any clinical use as it would appear that the Examiner would require.

Applicants draw the Examiner's attention to the various *in vitro* assays disclosed in the specification, such as inducing a specific CTL response *in vitro* as well as measuring the CTL response from, *e.g.*, patient samples (Example 16 and 17). The Examiner stated the uses of Example 16 are not enabled because the specification allegedly does not "provide guidance as to which disease or disorders the peptides and proteins can be used as reagents to procure a diagnosis or prognosis". Office Action at page 11. The Examiner further asserted that not all "tumor-markers" are diagnostically

reliable, though Applicants remind the Examiner that the claimed invention does not need to be diagnostically reliable to have an enabling use.

Applicants assert that the claimed peptides can be used to elicit a specific immune response, particularly from CTL (*see* Example 3 and Table XXIV) which can be used for further research into prostate cancer or other diseases. Among other uses, these peptides can be used to measure whether isolated CTLs, such as from a prostate cancer patient, recognize the claimed peptide (Example 17). Since this peptide is an epitope of PAP, a well-known cancer marker (*see e.g.*, Van Etten, made of record by the Examiner), it is useful to know if a patient's CTL recognize this epitope. If it does, then the claimed peptide may potentially be used to increase the immune system's response to this epitope. If there is no native recognition of the claimed peptide, then these peptides may be used to "break tolerance" and induce an immune response to this peptide.

Enablement is not precluded if some experimentation is required so long as it is not "undue". *In re Wands*, 585 F.2d 731, 737 (Fed. Cir. 1988). In *Wands*, the court held that a specification was enabling for obtaining antibodies needed to practice the invention because it contained considerable guidance, there was a high level of skill in the art, and all methods to needed to practice the invention were well known. Applicants note that obtaining antibodies is not a trivial exercise, but yet it was considered routine. Like in *Wands*, a person of skill in the art for the claimed invention has a doctorate or equivalent and would easily be able to identify whether a given peptide claimed herein would have the requisite binding and/or immunogenicity for desired use. First, binding assays can be performed to screen candidates as described in Example 1. Then successful candidates can be further screened, if necessary, using the methods of Example 3. Further, the specification cites art teaching these methods. Thus, like in

Wands, the skill in the art is high, the specification provides ample guidance and all methods needed are well known.

The Examiner is also reminded of *Ex parte Mark*, 12 USPQ2d 1905 (BPAI), which stands for the proposition that claims directed to a "biologically active" protein are enabled if, at the time of filing, it would have been routine for the skilled artisan to identify such a protein using a conventional screening assay, which Applicants assert the methods of Examples 1 and 3 are. Thus, the fact that any *given* candidate polypeptide might not have binding or immunogenic activity does not militate against a conclusion of enablement provided that one skilled in the art could have readily assayed even a large number of candidates to find at least a reasonable number of "winners". Indeed, Schoel, cited by the Examiner as an example of the unpredictable binding of epitopes, actually supports the opposite legal conclusion. Half of the peptides tested showed good binding, which does not indicate that the desired binding is a rare event. Applicants assert that a fifty percent success rate yields a very reasonable number of winners, thus supporting enablement.

For all these reasons, it is respectfully submitted that at least one disclosed use is enabled, and thus the enablement rejection should be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 124-127, 131, 135-137, 139, 215 and 230 were rejected under 35 U.S.C. § 112, second for allegedly being indefinite. Specifically, the Examiner asserted that the additional elements of these claims added to SEQ ID NO:6827 exceeds the 15 amino acid length as previously recited in claim 114. Applicants respectfully traverse this rejection as it may apply to the amended claims.

Without acquiescing to the rejection, claim 114 has been amended to no longer recite the 15 amino acid length limitation. Claims 121-123 and 126 have been cancelled. Applicants point out the additional elements of claims 124, 125 and 127 are "linked to" SEQ ID NO:6827. Thus, these claims read on the peptide of claim 114 and something else (T helper peptide, spacer molecules or a lipid), as a limitation on claim 114. Likewise, the polymers of claims 129 and 130 are merely added limitations by reciting additional peptides, either the same peptide or different immunogenic peptides. *See* page 46, lines 16-17. The composition claims are similar in that they recite SEQ ID NO:6827 plus an additional element or limitation by including a carrier (claim 131), one or more isolated peptides (claim 131), etc. Therefore, addition of these elements do not contradict the limitations of claim 114 and are not indefinite. Therefore, Applicants respectfully request that the rejection be withdrawn.

Claims 125 and 139 were rejected for allegedly being indefinite for reciting "linker". However, the Examiner notes there is guidance for the term "spacer", which the claims have been amended to recite. Ample guidance for the meaning of "linked by one or more spacer molecules" and "linked by one or more spacer amino acids" can be found, *inter alia*, on page 54, lines 4-15 of the specification. Therefore, Applicants respectfully request that the rejection be withdrawn.

Claims 131 and 137 were rejected as allegedly being indefinite for reciting "carrier". Applicants note that amended claim 131 is drawn to a composition comprising a peptide (SEQ ID NO:6827) and "a carrier molecule". Claim 137 is similar as it is drawn to a composition of claim 135 (comprising SEQ ID NO:6827 and one or more other isolated peptides) and further comprising a carrier molecule. Such carrier molecules are described on page 46, lines 24-33. A person of skill in the art would easily

distinguish these carriers from the "pharmaceutically acceptable carrier" of claim 140 and described on page 59, lines 12-24 as a solution into which to dissolve or suspend the claimed peptide. A person of skill in the art would readily understand the difference between a carrier molecule as recited in claims 131 and 137 from a pharmaceutically acceptable carrier. Therefore, claims 131 and 137 comply with 35 U.S.C. § 112, second paragraph, and Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 130, 135-137 and 140 were rejected under 35 U.S.C. § 102 for allegedly being anticipated by Van Etten *et al.* as evidenced by WO 94/20127. Specifically, the Examiner asserts that Van Etten teaches a cDNA encoding PAP comprising SEQ ID NO:6827, and WO 94/20127 teaches that SEQ ID NO:6827 is a fragment of PAP. Applicants respectfully traverse the rejection as it may apply to the amended claims.

Without acquiescing to the rejection, claim 130 has been amended to be directed to a heteropolymer of SEQ ID NO:6827 and "at least one different immunogenic peptides, wherein said peptides are immunogenic." A heteropolymer of SEQ ID NO:6827 and a <u>different</u> immunogenic peptide cannot encompass the native PAP protein disclosed in Van Etten.

Claim 135 has been amended to recite a composition comprising SEQ ID NO:6827 and "one or more other isolated peptides". As these other peptides are isolated, this claim cannot read on the native PAP peptide as taught by Van Etten. Claim 136 recites that the peptide is linked by one or more spacer molecules, which is not taught by Van Etten. Finally, claims 137 and 140 as well as other claims dependent from claim 135 also incorporate the limitation that the other peptides are isolated, and thus are not

anticipated by the native PAP sequence of Van Etten. Because none of these claims are anticipated by the cited references, Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 126, 128, 130, 135-137, 139 and 140 were rejected under 35 U.S.C. § 103 for allegedly being unpatentable over Van Etten *et al.* as evidenced by WO 94/20127 and in view of Zsebo and Ostanin *et al.* Specifically, the Examiner alleged these claims read on fusion proteins of SEQ ID NO:6827 with some other heterologous peptide and that the cited art teaches a fusion comprising PAP, a spacer and prepro-α-factor, as well as compositions thereof. Applicants respectfully traverse this objection as it may apply to the amended claims.

The recited art does not teach each and every element of the claimed invention. Without acquiescing to the rejection, claims 126, 128 and 130 were cancelled, leaving amended claims 135-137, 139 and 140 as currently rejected. Claim 135 has been amended to recite a composition comprising SEQ ID NO:6827 and "one or more other isolated peptides". Claims 136, 137, 139 and 140 depend from claim 135 and thus incorporate this limitation of the other peptides being isolated. Further, because these claims add limitations that the fragment SEQ ID NO:6827 is linked to the other isolated peptides using spacer molecules (claim 136) or spacer amino acids (claim 139), they are even less able to read on a full-length protein. As SEQ ID NO:6827 and other isolated peptides do not comprise the full-length PAP protein, these claims cannot read on the native PAP peptide as taught be Van Etten as evidenced by WO 94/20127. Ostanin cannot remedy this deficiency as it only teaches wild type PAP as well, not SEQ ID

NO:6827 and "one or more isolated peptides". Zsebo only teaches fusion proteins in general. Indeed, the Examiner states that the combination of references teach a fusion comprising PAP, a spacer and prepro-α-factor, as well as compositions thereof. Thus, none of the art alone or in combination teach each and every element of the claimed invention.

Since the cited references do not teach each and every limitation of the claimed invention, there can be no motivation to combine these references to achieve the claimed invention, nor any expectation of success in such a combination. Therefore, Applicants assert that a *prima facie* case for obviousness has not supported, and respectfully request that the rejection be withdrawn.

Double Patenting

Claims 114, 121-128, 130, 131, 133-137, 139, 140 and 215 have been provisionally rejected under the doctrine of obviousness-type double patenting over claims 1-14 and 23-25 of U.S. Appl. No. 10/168,507. Applicants respectfully traverse this provisional rejection, but request that the rejection be held in abeyance until such time the conflicting claims may be patented.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for

allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Attachment A
Appl. No. 09/633,364

Paper No. 17

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte DANE K. FISHER, and RAGHUNATH V. LALGUDI

Appeal No. 2002-2046
Application No. 09/619,643

HEARD: March 16, 2004

Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claim 1, the only claim pending in the application, reproduced below:

1. A substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO:5.

The examiner does not rely on a reference.

GROUNDS OF REJECTION

Claim 1 stands rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility. Claim 1 also stands rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to provide an adequate written description of the claimed invention. We affirm the utility and enablement rejections. We reverse the written description rejection.

BACKGROUND

The subject matter of the present appeal is directed to expressed sequence tags (ESTs). See Specification, page 15, lines 9-10. ESTs "are short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones." Specification, page 1.

As set forth at page 9, lines 2-4, of appellants' specification "[t]he present invention provides a substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 32236." Of these 32,236 nucleic acid sequences, the originally filed claims where directed to SEQ ID NO: 1 through SEQ ID NO: 4,013. On January 26, 2001 (Paper No. 4), the examiner entered a Restriction requirement into the record, requiring, inter alia, appellants "to elect up to 5 nucleic acid sequences" for consideration on the merits. Paper No. 4, page 3. In response, appellants elected SEQ ID NO:1 through SEQ ID NO:5. The ESTs set forth in SEQ ID NO: 1 through SEQ ID NO:

5 are disclosed to be obtained from cDNA library LIB3115 "generated from maize (RX601, Asgrow Seed Company, Des Moines, Iowa U.S.A.) pooled leaf tissue...." Specification, pages 79-80, Example 1.

The specification sets forth a number of utilities for the nucleic acid molecules of SEQ ID NO: 1 through SEQ ID NO: 5 which are summarized by the examiner (Answer, bridging paragraph, pages 5-6) as follows:

> The specification teaches that the nucleic acids may be used to produce a plant containing reduced levels of a protein (pg. 11), determining an association between a polymorphism and a plant trait (pg. 11), isolating a genetic region or nucleic acid (pg. 11), determining a level or pattern in a plant cell of a protein in a plant (pg. 11), determining a mutation in a plant whose presence is predictive of a mutation affecting a level or pattern of a protein (pg. 13), as molecular tags to isolate genetic regions, isolate genes, map genes, and determine gene function (pg. 14), and identifying tissues (pg. 14)[.] The specification states that the nucleic acid ESTs of the present invention can enable the acquisition of molecular markers, which can be used in breeding schemes, genetic and molecular mapping and cloning of agronomically significant genes (pg. 31).

In the examiner's opinion "[t]hese are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the nucleic acids being claimed." Answer, page 6. For example, the examiner finds (Answer, page 10), "determining whether the claimed nucleic acids have or do not have a polymorphism would require determining whether there was a polymorphism within such a sequence and then determining how to use this information in a patentably meaningful way."[1]

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[1] During the Oral Hearing, appellants' representative confirmed that the administrative file contained no evidence that the claimed ESTs where capable of detecting a polymorphism that correlated with any particular trait.

In presenting their case on appeal, appellants focus on use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, and their use as probes or as a source for primers. See e.g., Brief, pages 6-12. According to appellants (Brief, page 3), "they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example the ability to identify the presence or absence of a polymorphism in a population of maize plants." Furthermore, appellants assert (Brief, page 8), "[t]he specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...."

CLAIM CONSTRUCTION

As set forth above, claim 1 on appeal is drawn to a substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO:5. According to appellants' specification (page 15, lines 19-25), the term "substantially purified"

> refers to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

As we understand the claimed invention the use of the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of

the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5, but instead only allows for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5.[2] In this regard, we recognize, as does the examiner (Answer, page 14), the claim as written encompasses, inter alia, genes, full open reading frames, fusion constructs, and cDNAs.

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, selected from the group consisting of the nucleic acid molecule defined by the 429 nucleotide sequence set forth in SEQ ID NO: 1, the 413 nucleotide sequence set forth in SEQ ID NO: 2, the 365 nucleotide sequence set forth in SEQ ID NO: 3, the 414 nucleotide sequence set forth in SEQ ID NO: 4, and the 333 nucleotide sequence set forth in SEQ ID NO: 5, with or without any preceding or trailing nucleotides, or other molecules.

DISCUSSION

Utility

The starting point for determining whether a nucleic acid molecule selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 5

[2] This interpretation of the claimed invention was confirmed by appellants' representative during the Oral Hearing.

possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in Brenner, at 534-35, 148 USPQ at 695[3],

> the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

In considering the issues presented in this appeal, special attention must be paid to the Brenner court's statement that a patent should issue only when an invention possesses "substantial utility," i.e., "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a

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[3] In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, have used the phrases "substantial utility" and "practical utility" interchangeably. See e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1963-1964, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

> [i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.[4]

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

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[4] The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of

§ 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the

researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in

cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by "marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar

compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use

as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 35-42 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5. To the contrary, according to appellants' specification (page 35, lines 25-26), "one or more of the [32,236] EST nucleic acid molecules (or a sub-fragment thereof) may be employed as a marker nucleic acid molecule to identify ... polymorphism(s)." The specification does not explain why any of the 32,236 nucleotide molecules disclosed in the specification, or more specifically the five nucleotide molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5, would in fact be useful in detecting polymorphisms.

Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that an EST by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, bridging paragraph, pages 10-11):

> Polymorphisms are natural variations within sequences which themselves may not have any meaningful use. Therefore, determining whether the claimed nucleic acids [(or nucleic acids detected by the claimed nucleic acids)] have or do not have a polymorphism would require determining whether there was a polymorphism within such a sequence and then determining how to use this information in a patentably meaningful way. The [a]ppellant also argues, "many of these uses are directly analogous to a microscope". This argument has been reviewed but is not convincing because the microscope provides information to the scientist which is automatically useful. For example, the microscope may be used for identification and differentiation between gram-positive and gram-negative bacteria. The differentiation of bacteria facilitates in the administration of proper antibiotics. For example, if the microscope is used to determine whether Staph is present or whether Strep is present provides valuable information to the scientist and/or doctor for treating patients. The instant invention, however, provides no information to this extent. If the scientist determines that SEQ ID NO: 1 is present, the scientist does not know how to use this information. Thus, the identification of SEQ ID NO: 1 is not a substantial utility.

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the EST is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further

define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

b. Probes or source of primers

Appellants argue that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...." Appeal Brief, page 8. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or phenotype to any of the nucleotide molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 5. In the absence of such information, using the claimed molecules to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.

Appellants also assert that the claimed nucleic acid molecules may be used in a "chromosome walk." Brief, pages 8-9. According to appellants (Brief, page 9),

> The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in leaves at the time of anthesis. Isolation of such a promoter would be desirable and particularly useful because it allows expression of proteins at that important developmental state, including proteins that provide disease resistance. Because the claimed nucleic acid molecules were isolated from leaves, they provide an appropriate starting point for isolating a promoter active in leaves. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. . .

As we understand this argument, the claimed ESTs may be useful in searching for promoters that are only active in leaves at the time of anthesis. The

specification, however, fails to demonstrate that any of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 5 would be useful in obtaining a successful result from such a search. As set forth at page 34, lines 14-19 of appellants' specification,

> The [32,236] nucleic acid molecules of the present invention may be used to isolate promoters of tissue enhanced[,] tissue specific, cell-specific, cell –type, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

The specification does not provide any expectation of successfully using any of the 32,236 nucleic acid molecules disclosed in the specification, or more specifically the five nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5, to isolate promoters of tissue enhanced, tissue specific, cell-specific, cell–type, developmentally or environmentally regulated expression profiles.

Furthermore, notwithstanding appellants' assertion (Brief, page 9), there is no evidence on this record that any of the nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5 are tissue or cell-type specific, or developmentally or environmentally regulated. In this regard, we note that the claimed nucleic acid molecules were isolated from the cDNA library LIB3115. Specification, page 80, lines 5-6. There is no evidence on this record that LIB3115 is a subtractive cDNA library, wherein nucleic acid molecules from other maize tissue, or from other developmental stages, was subtracted (removed)

from the library. Compare, for example, the subtractive cDNA library LIB3153 which is disclosed (specification, page 83, lines 17-19) to be "generated by subtracting driver cDNA, which is prepared from kernels harvested from 15 DAP [days after pollination] maize plants, from target cDNA, which is prepared from endosperms harvested from 5-8 day[s] after pollination (DAP) maize plants." In contrast to the claimed nucleic acid molecules, nucleic acid molecules SEQ ID NO: 24,931 through SEQ ID NO: 25,680 are from the subtractive cDNA library LIB3153.

In our opinion, the claimed nucleic acid molecules having the sequences identified as SEQ ID NO: 1 through SEQ ID NO: 5, represent five randomly selected nucleic acid molecules isolated from pooled leaf tissue at the time of anthesis. Notwithstanding appellants' emphasis on "anthesis," for the foregoing reasons, we find no evidence on this record that any of appellants' five randomly selected nucleic acid molecules are expressed only at the time of "anthesis." Accordingly, despite appellants' assertion to the contrary, there is no reasonable expectation that any of the claimed nucleic acid molecules would be capable of isolating a promoter that was only active in leaves at the time of anthesis. As appellants recognize (Brief, page 9), "[a] random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter" compared to a nucleic acid molecule that is known to be specifically associated with this stage of plant development.

We recognize appellants' argument (Brief, bridging sentence, pages 9-10), "[a]n invention may be 'less effective than existing devices but nevertheless

meet the statutory criteria for patentability.' Custom Accessories, Inc. v. Jeffrey-Allan Indus., 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986)." While we agree with appellants' statement, we fail to see how it applies to appellants' claimed invention, wherein there is no evidence or expectation that the claimed nucleic acid molecules would be "effective" at all. In this regard, we remind appellants that an invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695.

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

c. Other Arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Brief, page 6. Specifically, appellants argue (id.) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which appellants assert to have a "legally sufficient utility." Id.

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portion of the specification cited in support of this argument (page 73, line 17 through page 74, line 17) indicates that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in the suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to be used is uncharacterized[5] as here. Such a use does not provide a specific or substantial benefit in currently available form.

Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology

[5] To emphasize the uncharacterized nature of appellants' invention we note the examiner's finding (Answer, page 17) that translating SEQ ID NO: 5 in all 6 possible reading frames reveals that the sequence contains numerous stop codons which would terminate the translation of a protein, or protein fragment, encoded thereby.

and use as molecular markers. Brief, page 6. In regard to microarrays, appellants argue (id. fn. 3) that it is "standard practice" to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. We find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in e.g., SEQ ID NO: 1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the SEQ ID NO: 1-specific information derived from a gene expression experiment would mean. As the examiner points out (Answer, page 9), "the instant claimed nucleic acids appear to require further experimentation on the material itself to determine the function and properties of the claimed nucleic acids."

To highlight the examiner's assertion, suppose, for example, that a researcher found that SEQ ID NO: 1 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO: 1 expression would depend on other factors, but again the specification provides no hint as to what other factors

might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using SEQ ID NO: 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use SEQ ID NO: 1-specific gene expression data.

Assuming arguendo, that a generic gene expression assay—one based on monitoring expression of thousands of uncharacterized nucleic acids would provide a useful tool for, e.g., drug discovery, it does not follow that each one of

the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard. The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5 are

useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of SEQ ID NO: 1 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 11. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecules of SEQ ID NO: 1 through SEQ ID NO: 5 in such devices represents a substantial use.

For the foregoing reasons we affirm the rejection of claim 1 under 35 U.S.C. § 101.

Enablement

According to the examiner (Answer, page 13, emphasis removed), "since the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility for the reasons set forth [in support of the rejection under 35 U.S.C. § 101] one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, page 12), this rejection should be reversed for the same reasons set forth in their arguments regarding the

rejection under 35 U.S.C. § 101. Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph.

Written description

This rejection stands on a different footing. As we understand the examiner's argument the use of the transitional phrase "comprising" in appellants' claimed invention results in appellants claiming a large genus of nucleic acid molecules which are not adequately described by SEQ ID NO: 1 through SEQ ID NO: 5. Answer, pages 13-16. Apparently the examiner is of the opinion that the claimed invention should be limited to nucleic acid molecules as set forth in SEQ ID NO: 1 through SEQ ID NO: 5. In response appellants argue (Brief, page 14, original footnote omitted),

> Applicants have provided the nucleotide sequences required by the claims, i.e., SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, and SEQ ID NO: 5, and have thus established possession of the claimed invention. The fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences[6] does not mean that [a]pplicants were any less in possession of the claimed nucleic acid molecules.

As discussed supra, as we understand the claimed invention, the use of the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences set forth in SEQ ID NO: 1

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[6] By way of examples appellants explain (Brief, bridging paragraph, pages 14-15) that the specification discloses, inter alia, the claimed nucleic acid molecules joined together with vectors, and other nucleic acids (e.g. fusion nucleic acid molecules) and detectable labels.

through SEQ ID NO: 5, but instead only allows for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5. We agree with appellants that they have provided an adequate written description of nucleic acid molecules with the sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5. That the claimed nucleic acid molecules may have other molecules attached to either, or both of their 5' or 3' ends does not diminish appellants' adequate written description of the nucleic acids molecules with the sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5 as claimed.

Accordingly, we reverse the rejection of claim 1 under the written description provision of 35 U.S.C. § 112, first paragraph.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

William F. Smith
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

) BOARD OF PATENT
) APPEALS AND
) INTERFERENCES

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